REMARKS

I. STATUS OF THE CLAIMS

With entry of this supplemental amendment, claims 1, 4, 5, and 7 are currently pending. Claims 1 and 7 are amended and claim 6 is canceled herein. Support for the amendments to claims 1 and 7 can be found in the specification at least on page 6 and in the original claims. With respect to the dose range added to claim 1, support for this amendment can at least be found on page 6 of the present specification. Concerning this amendment, Applicants submit that they are entitled to claim less than the full scope of their original disclosure. *See In re Johnson*, 194 U.S.P.Q. 187 (C.C.P.A. 1977). No new matter is added by these amendments.

II. REJECTION UNDER 35 U.S.C. § 103

The Office continues to reject claims 1 and 4-7 under 35 U.S.C. § 103 as unpatentable over RO 92436 to Buzas et al. ("Buzas"). Office Action dated August 17, 2005; Office Action dated February 26, 2004; Office Action dated August 14, 2003 at page 6. Applicants continue to respectfully disagree for the reasons of record and for the additional reasons provided below.

As shown in Table 3, Buzas examines the administration of pindolol at 3 mg/day over the course of a 10 day treatment by measuring the production of hydrochloric acid and the activity of carbonic anhydrase in the gastric mucosa as well as in red blood cells. Buzas at page 8. It is this teaching the Office relies on, *inter alia*, to establish a *prima facie* case of obviousness. *See* Office Action at page 3 and 5. As detailed in the Response filed November 7, 2005, Buzas' teachings when viewed "as a whole" are directed to the reduction of gastric acid secretion for the treatment of gastritis,

gastroduodenitis, and gastric and duodenal ulcers. *See* Amendment and Response filed on November 7, 2005, at pages 5 and 6. In contrast, amended independent claim 1 not only recites gastrointestinal diseases outside the scope of Buzas, but also a composition outside the scope of Buzas.

For example, the present claims are directed to "at least one gastrointestinal disease [that] exhibits symptoms that *lack a structural or biochemical abnormality of the gastrointesntial tract*, and . . . [are] chosen from non-ulcerative dypepsia, irritable bowel syndrome, cancer chemotherapy-associated disorders of motility, and combinations thereof." Buzas clearly states on page 4 that "the object of the present invention is to obtain a synergistic pharmaceutical composition . . . through vasomotor impulse regulation of *gastric secretions*." Gastric acid secretions occur in the "gastric glands in the fundic area of the gastric mucosa [i.e., the lining of the stomach] . . . ." Buzas at page 5. Because the stomach is part of the gastrointestinal tract and the present claims recite treating gastrointestinal diseases that "*lack a structural or biochemical abnormality of the gastrointestinal tract*," Buzas fails to teach or suggest all the elements of the present claims. *See* M.P.E.P. § 2143 (8th ed., Rev. 3, 2005).

With regard to Buzas' composition, as detailed in the Response filed July 6, 2005, Buzas teaches a "*synergistic*" composition of a carbonic anhydrase inhibitor *and* a beta-adrenergic blocker. Buzas at Abstract, and page 2. There simply is no clear and particular suggestion in the cited prior art to modify Buzas by omitting a carbonic anhydrase inhibitor from a composition intended for use in treating gastrointestinal disorders. Buzas describes a *synergistic* composition containing a carbonic anhydrase inhibitor and a beta-adrenergic blocker in specific weight ratios. Buzas at page 2.

According to Buzas, the object of the invention is to obtain a synergistic composition through the "selection of ingredients and the mixture ratio thereof." *Id.* Accordingly, the addition of a carbonic anhydrase inhibitor would materially alter a composition "consisting essentially of an effective amount of S(-)pindolol," as recited in the presently claimed invention, by producing a synergistic effect different from the effect of S(-)pindolol alone. Given this synergy, Applicants contend that the addition of carbonic anhydrase inhibitors would materially affect the basic and novel characteristics of the claimed invention. As the Office acknowledges, any elements having such an effect are excluded from a claim that recites, "consisting essentially of." *See* Advisory Action dated June 1, 2004; *see also*, *PPG Industries v. Guardian Industries Corp.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998).

Even if one considers Buzas at Table 3 where pindolol is administered alone, Buzas uses a dose of 3 mg/day. Buzas at page 8. Furthermore, Buzas at Table 3 measures hydrochloric acid and carbonic anhydrase in patients with gastroduodenal disorders. *Id.* He concludes that beta-blockers, including pindolol, demonstrate "slightly decreased" production of gastric acid and carbonic anhydrase. *Id.* Buzas, however, does not associate these "slightly decreased" values with exhibiting a therapeutic effect. *Id.* In fact, Buzas finds therapeutic effects only with the combination of carbonic anhydrase inhibitors and beta-adrenergic blockers. *Id.* at page 11 and Table 9 at page 12.

In contrast, the present claims recite an effective amount of pindolol outside the dose used in Buzas, i.e., ranging from greater than 3 mg/day to about 50 mg/day. Considering the dose in Buzas along with the results Buzas presented (i.e., beta-

blockers when used alone are ineffective as treatment), Buzas fails to provide any guidance or suggest or motivate a person of ordinary skill in the art to use a beta-blocker as a mono-therapy for gastrointestinal conditions, let alone increase the dose. Proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. M.P.E.P. § 2146(X) (citing *In re Hedges*, 783 F.2d 1038, 228 U.S.P.Q. 685 (Fed. Cir. 1986)).

For at least these reasons, a *prima facie* case of obviousness has not been established and as such, Applicants respectfully request the withdrawal of the rejection.

III. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

If the Examiner believes a telephone call could be useful in resolving any outstanding issues, the Examiner is urged to contact Applicants' undersigned representative at 202.408.4345.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: December 29, 2005

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